

**AMENDMENTS TO THE SPECIFICATION:**

Please amend page 4, line 34-page 5, line 22, as follows:

1) Assay for increase of vascular permeability: A golden hamster, weighing 65-100 g, is anaesthetized with a mixture of ~~Apozepam~~APOZEPAM<sup>®</sup> (Diazepam 5 mg/ml Apothekarnes Laboratorium, Oslo, Norway) and ~~Mebumal-Vet~~MEBUMAL VET<sup>®</sup> (Pentobarbital 60 mg/ml, NordVacc Vaccin AB, Malmö, Sweden) volume ratio 10:1. An initial dose of 0.3 ml is given intraperitoneally. Additional injections of 0.1-0.4 ml are administered each 30 minutes. The hamster is placed on a heated (37° C) perspex plate, and the right cheek-pouch is everted over a translucent rubber plate and covered with plastic film in order to prevent reduction in blood flow rate due to direct exchange of oxygen. An injection of 0.1 ml of FITC Dextran (mw 150.000, 25 mg/ml, Sigma, St Louis, USA) is made in the femoral vein for fluorescence vital microscopic observations of macromolecular extravascular leakage. Temperature and humidity is controlled by irrigation of saline at 37°C. An injection of approximately 0.02 ml of a suitable concentration of the substance to be tested is made between two layers of the cheek-pouch using a thin injection needle (diameter 0.4 mm). The same volume of saline is performed in an adjacent part of the cheek-pouch at a distance from the other injection site sufficient to eliminate the risk of communication between the saline and the substance within the cheek-pouch. The injection procedures are carried out under a stereomicroscope to minimize mechanical damage to the microvessels. Microvascular reactions are studied for 60 minutes at various magnifications, using fluorescence microscopic techniques (Leitz, Wetzlar, Germany). A pro-inflammatory cytokine as defined according to the present invention induces a leakage of the fluorescent macromolecule FITC-dextran. A similar leakage should not be observed at the site injected by saline.

Please amend page 5, line 23 - page 6, line 13, as follows:

2) Assay for leucotaxia or chemotaxia: A pig, bodyweight 25-30 kg, is anaesthetized with an intramuscular injection of 20 mg/kg bodyweight of ~~Ketalar~~KETALAR<sup>®</sup> (ketamine 50 mg/ml, Parke-Davis, Morris Plains, New Jersey) and an intravenous injection of 4 mg/kg bodyweight of ~~Hypnodil~~HYPNODIL<sup>®</sup> (methomidate chloride 50 mg/ml, AB Leo, Helsingborg, Sweden) and 0.1 mg/kg

bodyweight of ~~Stresnil~~ STRESNIL<sup>®</sup> (azaperon, 2 mg/ml, Janssen Pharmaceutica, Beerse, Belgium). Anaesthesia is maintained by additional intravenous injections of 2 mg/kg bodyweight of ~~Hypnodil~~ HYPNODIL<sup>®</sup> and 0.05 mg/kg bodyweight of ~~Stresnil~~ STRESNIL<sup>®</sup>. One ml of a fluid containing a sufficient concentration of the substance to be tested is placed, in a suitable concentration locally in its natural form, in slow-release preparations or by continuous administration by osmotic mini-pumps, in a specially designed titanium-chamber. The chamber is 5 mm high and has a diameter of 15 mm. The top could be dismounted and is perforated with 18 holes, each with a diameter of 1.4 mm. The chamber, together with one chamber with the same volume of saline, are placed subcutaneously in the lumbar region through separate incisions, with no communication between the chambers. After 7 days the pig is reanaesthetized similar to the first procedure. The chambers are harvested and the content of the chamber is placed in a test-tube together with 1 ml of Hanks' Balanced Salt Solution (Life Technologies, Paisley, Scotland). From this suspension, 100 µl is used to wash out the chamber for remaining cells. This procedure is repeated 5 times. The test-tube is then shaken for 15 seconds. A total of 25 µl of the suspension and 25 µl of Türk's staining medium (Sigma, St Louis, USA) are mixed and placed in a chamber of Bürker. The total number of leukocytes in each chamber is determined using light microscopy. The chamber with a pro-inflammatory cytokine as defined according to the present invention then contains significantly more white blood cells than the chamber with only saline.

Please amend page 10, lines 1-3, as follows:

- Phosphodiesterase I, II, III, IV, and V-inhibitors, e.g., CC-1088, Ro 20-1724, rolipram, amrinone, pimobendan, vesnarinone, SB 207499 (cilomilast) (~~Ariflo~~ ARIFLO<sup>®</sup>)
- Melancortin agonists, e.g., HP-228

Please amend page 10, lines 28-33, as follows:

- Specific IL-1 $\alpha$  and IL-1 $\beta$  blocking substances, such as:
  - Monoclonal antibodies

- Soluble cytokine receptors
- IL-1 type II receptor (decoy RII)
- Receptor antagonists; IL-1ra, (~~Orthogen~~ORTHOGEN<sup>®</sup>, ~~Orthokin~~ORTHOKIN<sup>®</sup>)
- Antisense oligonucleotides